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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/132,521	08/11/1998	YOSHIYUKI NAGAI	50026/008001	9549

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EXAMINER
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ART UNIT	PAPER NUMBER
1632	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/132,521	Nagai et al.
Examiner	**Art Unit**
Joseph T. Woitach	1632

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Sep 3, 2002*

2a) ___ This action is **FINAL**. 2b) X This action is non-final.

3) ___ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-8, 10-12, and 14-23* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ___ Claim(s) _____ is/are allowed.

6) X Claim(s) *1-8, 10-12, and 14-23* is/are rejected.

7) ___ Claim(s) _____ is/are objected to.

8) ___ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) X The specification is objected to by the Examiner.

10) ___ The drawing(s) filed on _____ is/are a) ___ accepted or b) ___ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ___ The proposed drawing correction filed on _____ is: a) ___ approved b) ___ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ___ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ___ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ___ All b) ___ Some* c) ___ None of:

1. ___ Certified copies of the priority documents have been received.
2. ___ Certified copies of the priority documents have been received in Application No. _____ .
3. ___ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ___ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ___ The translation of the foreign language provisional application has been received.

15) ___ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) X	Notice of References Cited (PTO-892)	4)	Interview Summary (PTO-413) Paper No(s).
2)	Notice of Draftsperson's Patent Drawing Review (PTO-948)	5)	Notice of Informal Patent Application (PTO-152)
3)	Information Disclosure Statement(s) (PTO-1449) Paper No(s).	6)	Other:

Continued Prosecution Application

The request filed on July 3, 2002, paper number 25, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/132,521 is acceptable and a CPA has been established. An action on the CPA follows.

DETAILED ACTION

This application is an original application filed August 11, 1998.

Applicants' amendment filed September 3, 2002, paper number 26, has been received and entered. Claims 9 and 13 have been canceled. Claims 1-3, 6-7, 10-12, 14 and 15 have been amended. Claims 16-23 have been added. Claims 1-8, 10-12, 14 and 15-23 are pending and currently under examination.

Specification

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). Specifically, the specification contains amino acid sequences (for example page 10, lines 3 and 27) and polynucleotide sequences (figure 1) which are not identified by SEQ ID NOs. Additionally, with respect to figure 1, the figure or the Description of the Drawings should be amended to reflect the SEQ ID NO.

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 11, 12 and 15 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

It is noted that the instant claims have been amended and now encompass the transfection of cells *in vitro*, and use of said cells *in vitro* (claim 15) or for the treatment of HIV in a subject (claim 10). The art teaches that a subject with HIV can be treated by the administration of a variety of chemokines either alone or in various combinations. Given that one of skill in the art can easily transfect a target cell of interest *in vitro*, and assay the for the production of a transgene producing a chemokine for appropriate "therapeutic" amount of production in said cell, it would not constitute an undue burden to practice the method as instantly claimed.

Additionally, because the pharmaceutical products of claims 11 and 12 can be used in these methods, they are accorded one enabled use and meet the enablement requirements of 35 USC 112, first paragraph.

Claims 1-8, 10-12, 14 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

In the instant case, the recitation of "soluble" is considered new matter. Applicants point to page 11, lines 8-11, as an example for support of the new amendment. Upon review of this portion of the specification, Examiner can find no literal support for this embodiment. Further, though the single example of SDF-1α is disclosed as being secreted into the culture supernatant, there is insufficient description or evidence to indicate that the secreted protein was soluble or if the solubility of SDF-1α would extend to any other expressed protein or chemokine. It is noted that the disclosure does not provide any specific sequences for the chemokines contemplated and relies on the art to practice the claimed invention. Further, the disclosure provides no guidance or discussion for modifications of sequences known in the art, in particular modifications or means to make the sequences "soluble", if in fact they would not be soluble. Thus, in light of the

teaching in the teaching of the present specification and the art of record, the embodiment of "soluble" is considered new matter.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1-8, 10-12, 14 and 15-23 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 11, 12, 14 and 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 1, 6, 11, 12 and dependent claims, are unclear and confusing in the recitation of "Sendai virus vector expressing" a chemokine because a virus or virus vector by itself can not express a protein. It is only in the context of a infected or transfected cell that a virus is capable of expressing a protein. The metes and bounds of the claims are not defined because it is unclear if the claim is directed only to a viral vector or would include the vector in the context of a cell wherein a protein can be expressed.

Claims 8, 17, 18 and dependent claims, recite the limitation "removing virions" in the additional method step. There is insufficient antecedent basis for this limitation in the claim because the independent claims are only drawn to the use of a viral vector and there is no indication or requirement that a virion is specifically used or is formed during the process of producing a protein. Further, even in the context of expression in a cell (see rejection above) the claims clearly encompass the use of non-disseminative and non-replicating viral vectors and in these cases neither would form a virion.

Claims 15, 22 and 23 are vague and unclear in the recitation of "inhibiting proliferation of HIV-infected cells" because in light of the teachings of the present specification and the art of

record, the antiviral activities of chemokines is directed to viral replication, not the cell which is infected. It is unclear if the claims are directed to affecting the cell proliferation, viral proliferation, or proliferation of only infected cells.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 6, 7, 11, 14, 16, 20 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Shioda *et al.* (AIDS Res, 11:167, 1997)

Shioda *et al.* teach a Sendai viral vector which expresses a biologically active CXC-chemokine SDF-1α (claims 1-3, 6, 7). Shioda *et al.* teach that the sequence encoding SDF-1α is inserted proximal to the N gene, therefore it would not disrupt the ability of the virus to replicate or disseminate (claims 4, 11). The SDF-1α protein is made by virtue of the expression of the viral vector in a host CEF cell line (claims 6, 7, 14, 16, 20, 21). Shioda *et al.* teach each of the limitations set forth in the claims, and thus, anticipates the claimed invention.

Additionally, with respect to the declaration of Yoshiyuki Nagai filed under 37 CFR 1.132, (filed March 16, 2001, attachment to paper number 17) this declaration is insufficient

to overcome the instant rejection because the cited Shioda *et al.* reference contains two additional authors, Matsushima and Uchiyama, which are not discussed in the declaration and thus, the Shioda *et al.* reference constitutes prior art (*In re Katz*, 687 F.2d 450 (CCPA 1982)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10-12, 14 and 15 stand rejected and newly added claims 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu *et al.* and Bleul *et al.* in view of Hasan *et al.* (J. Gen. Vir. 78:2813-2820, 1997) and Czaplewski *et al.*

Applicants note that the claims have been amended to require that a "soluble" chemokine is produced, and that the new limitation distinguishes the present claims from that disclosed in the prior art. Applicants argue that in light of references inability to use a Sendai virus expression system to produce a soluble, biologically active chemokine, the references fail to

provide the motivation or an expectation of success. Applicants point to the working examples in the present disclosure as evidence that a soluble chemokine can be expressed, secreted and isolated from the culture media. Further the working examples demonstrate that the chemokines are capable of inhibiting HIV-1 proliferation. See applicants amendment pages 5-6. Applicants arguments and declaration have been fully considered but not found persuasive.

As previously noted, the results presented in Yu *et al.* clearly indicate that gp120 can be expressed by various cell types at various levels (see for example page 460; Table 1), and that the protein produced is a functional protein (see results in figure 4). Yu *et al.* conclude that the characteristics of the Sendai virus make it a useful tool for the delivery and expression of other polynucleotide sequences (page 463; second column). Examiner notes that Yu *et al.* does teach that expression of luciferase resulted in aggregation of the expressed protein, however contrary to the attempt by Yu *et al.*, Hasan *et al.* clearly teach that the Sendai virus is capable of expressing an active form of the luciferase protein (see results in Table 2 and Figure 2). It is noted that the present specification provides no specific sequences for the chemokines contemplated or specific vectors for expressing these sequences, and thus, relies on the art for these teachings. With respect to soluble chemokines, Czaplewski *et al.* teach that chemokines have been generated and that the structure of various chemokines have been characterized in detail indicating that '[N]ot all chemokines self-associate' (page 16078; top of first column). Applicants arguments that an aggregated form of luciferase was produced in the expression system of Yu *et al.* and that one of ordinary skill in the art would not expect other proteins to be successfully produced is

unpersuasive because chemokines have been successfully produced prior to the filing of the instant application. Further, because the present disclosure relies on the art for the specific sequences and vectors to practice the instantly claimed invention, the sequences disclosed in the cited references would anticipate the embodiments of the chemokine sequences and vectors required to practice the instantly claimed invention. Additionally, as discussed previously, aggregation of any given protein is an effect of external factors separate from the ability of the Sendai virus to express a given polynucleotide. Further, the art teaches that the Sendai virus has been used successfully to express other proteins in various cell types, and Yu *et al.* and Hasan *et al.* each specifically suggest that the Sendai virus will be "an excellent tool for foreign gene expression" (Hasan page 2819, final paragraph). Bleul *et al.* teaches that the SDF-1 had already been cloned and characterized (page 830; top of first column). Bleul *et al.* is relied upon for the teaching that the chemokine SDF-1 blocks HIV entry affecting HIV infection and the ability of the virus to replicated. In light of the specific motivation of Yu *et al.* and Hasan *et al.* teaching that Sendai virus has realistic utility and broad application in to express large amounts of a protein and the specific teaching evaluating the effect of and the specific teaching of Bleul *et al.* that SDF-1, it would have been obvious to one of ordinary skill in the art to combine the teachings to express and evaluate the effect of chemokines in various cell types. As detailed above, there would have been a reasonable expectation of success by one of ordinary skill in the art to express a soluble chemokine using a Sendai virus vector.

Therefore, for the reasons above and of record, the invention is *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Walker *et al.* (WO 94/08022) teach that (-)RNA viruses, family which Sendai virus belongs, are useful as a vectors for the delivery and the expression of a foreign gene (see entire disclosure and claim 1).

Amara *et al.* (J. Exp. Med 86(1):139-146, 1997) and Kinter *et al.* (PNAS 93:14076-14081, 1996) teach the ability of various chemokines to inhibit HIV replication.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630